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THE EFFECT OF AGE AT EXPOSURE UPON THE RADIATION INDUCED DENTAL DEFECT IN RATS

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ADMINISTRATIVE INFORMATION

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ABSTRACT

Exposure of the rat to ionizing radiation results in formation of defective tooth substance, which subsequently becomes visible at the gingival crest in the shaft of the continuously growing incisor. The present study is concerned with the effect of age at irradiation upon the severity and temporal distribution of the radiation-induced dental lesion. Male rats were irradiated with a high sublethal dose (215 rads) of fast neutrons at 31, 110, or 619 days of age. The typical lesion (a chalky zone extending the full width of the tooth) was observed in the exposed shafts of the incisors beginning in the second month post-irradiation. While all animals exhibited the lesion in all incisors, the character of the lesion and its time sequence varied markedly with age at irradiation. The severity of the radiation effect was greater in the youngest group, as indicated by a wider lesion and a greater incidence of animals with fractured incisors (68% vs 11 or 12% for the older groups). The time sequence of appearance, duration of visibility, and disappearance by attrition at the occlusal edge occurred earlier in younger animals. However, these temporal differences appear related primarily to anatomic and physiologic factors associated with age per se rather than to a differential intensity of radiation damage.

NON-TECHNICAL SUMMARY

The Problem

Exposure of rats to ionizing radiation causes damage to the tooth-forming tissues. Tooth substance formed before the tissues recover is abnormal in appearance: a white defective zone becomes visible at the gum-line some weeks after exposure, progresses toward the tip of the incisor as eruption continues, and is finally worn off through normal attrition. Even before its appearance at the gum-line, the defective zone is structurally weak, and broken teeth may result. This study is about the effect of age at irradiation upon this phenomenon.

The Findings

After irradiation with a less-than-lethal dose of neutrons (215 rads), the entire process of appearance, progression along the incisor, and disappearance occurred earlier in juvenile (31 days at irradiation) than in young (110 days) or old (619 days) adults. The juvenile group had a higher incidence of rats with broken teeth (68% vs 11 or 12% for adults). The time sequence differences among groups appear to be related principally to structural and/or functional differences characteristic of age, rather than to a greater intensity of radiation damage in younger animals.

INTRODUCTION

Beginning some 35 days after exposure of adult male rats to ionizing radiation, a macroscopically visible region of defective tooth formation becomes exposed at the gingival crest on the shaft of the continuously growing incisor (Castanera, et al., 1963). Morphologically, it appears as a white transverse zone occupying the full width of the incisor. This defective zone progresses distally as the tooth erupts, and disappears at the occlusal surface through the normal attrition process. Even before its appearance at the gingival crest, this defective area is structurally weak, and mechanical stress may result in a fractured tooth with subsequent undesirable sequelae. The radiation effects upon the odontogenic processes which result in this lesion have been summarized in a recent review (Kimeldorf, et al., 1962). The initial report was concerned primarily with the relative potencies of x-rays and neutrons in producing the defect, and with dose-time-incidence relationships. The present study is concerned with the effect of age at exposure upon the severity and temporal distribution of the radiation-induced dental lesion.

METHODS

Three groups of male Sprague-Dawley rats of the USNRDL strain were used in this study. A juvenile group was irradiated at 31 days of age, a young adult group at 110 days of age and an old adult group at 619 days of age. The median life span for unirradiated rats in this colony is approximately 700 days.

These rats were part of a larger study concerned with the late effects of irradiation, but none of the manipulative procedures used appeared to affect the pattern of dental injury. Although littermate non-irradiated controls were used for the late effects parameters, only the irradiated animals are considered here since this dental lesion does not occur in non-irradiated animals.

All rats were individually housed in suspended mesh cages, with meal food (Purina Lab Chow) in open containers and water supplied ad libitum. Special maintenance procedures were successful in preventing the appearance of any epidemic respiratory disease. The animals were exposed (whole-body) at the UCRL Crocker Laboratory cyclotron to fast neutrons, with a fission-like energy spectrum, obtained by the Be (p,n) B reaction. First collision dose was calculated from sulfur wafers exposed with each group of animals. The characteristics of this source (Tochilin and Kohler, 1958) and the method of dosimetry (Tochilin, et al., 1956) have been published. The dose was found to be 215 ± 10 rads for all three groups of animals. In terms of 30-day mortality, this dose is in the high sublethal range.

Beginning at about 4 weeks post-irradiation, each rat was examined visually at 3 or 4 day intervals until no more dental lesions were apparent. Presence and approximate location of a lesion, and the occurrence of fractures were recorded for each incisor at each examination.

RESULTS

All of the rats ultimately exhibited a lesion on all incisor teeth; however, the severity of the lesion varied with age at exposure. In Table I is shown the number of animals exposed at each age, and the proportion of rats with fractured incisors. By the criterion of fracture incidence, the severity of the lesion was very marked in the juvenile group in which 68% of the animals exhibited one or more fractured teeth. In the young and old adult groups the fracture incidence was only 11 and 12%, respectively. In addition, the width of the defect along the tooth varied with age. Typically, the defective zone was of the order of 3/16" wide in the juvenile group, 1/16 to 2/16" wide in the young adults, and appeared as a hairline in the old adults.

There appeared to be some influence of tooth fracture upon the time course of the lesion. The data from the juvenile group are considered for this purpose since only in this group were there sufficiently large numbers of animals with and without fractured teeth. Furthermore, in this group the fractured teeth were essentially limited to the mandibular incisors since even those four animals with one or both maxillary incisors broken also had one or

Age at Exposure (Days)	No. of Rats	Percent Rats with Fractured Incisors				
		Mandibular		Maxillary		One or More
		One	Both	One	Both	
31	78	45	23	4	1	68
110	76	5	0	4	3	11
619	41	7	0	0	5	12

Table I. Total incidence of animals with fractured incisors according to age at exposure. All groups exposed to 215 rads of fast neutrons.

both mandibulars broken. Analysis of the data by means of the median test (Siegel, 1956) indicates that there were significant ($p < 0.05$) effects of fracture in two instances: the lesion remained visible longer on the maxillary incisors (22 days) of animals with fractures than on either (a) their own mandibular incisors (17 days) or (b) the maxillary incisors of animals without fractured mandibular incisors (17 days). Animals without fracture retained the lesion on the mandibular incisors for 18 days. From the above considerations it appears that the effect of fracture on progression of the lesion is primarily in terms of a depression in rate of attrition of the opposing unbroken tooth.

Because of the effect of fracture on the progression of the dental lesion toward the occlusal edge, rats with teeth fractured at any time were excluded from analysis of the time sequence of the lesion. Figure 1 illustrates the effect of age at irradiation upon the time sequence of the dental lesion in both maxillary and mandibular incisors for all three age groups.

Regardless of age at exposure, the radiation-induced dental lesion appeared first upon the mandibular incisors and then upon maxillary incisors. In the juvenile group there was considerable overlap in time with respect to the incidence patterns for animals with lesions on mandibular and on maxillary incisors. In the curves for the two older groups there is a general spreading out and a shift

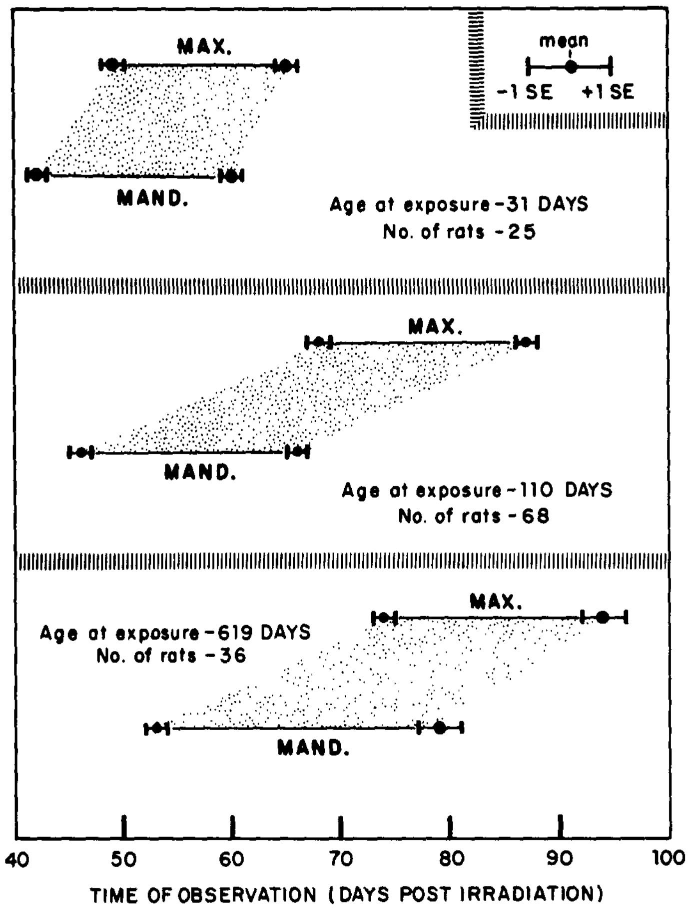

Fig. 1 Percent incidence of rats with one or more incisors exhibiting a lesion as a function of age at exposure and time post-irradiation. Radiation: 215 rads of fast neutrons (whole-body). Animals with fractured incisors are excluded.

to the right, particularly for the incidence of the lesion on maxillary incisors. Indeed, it was common in individual animals of these two groups to observe the complete cycle of appearance, progression, and disappearance of the lesion on mandibular incisors before the appearance of the lesions on maxillary incisors.

For purposes of description and comparison, the mean days post-irradiation of first and last observation, and net days of visibility for dental lesions are summarized in Fig. 2. Analysis by the median test (Siegel, 1956) indicates that for mandibular teeth, significant ($p < 0.05$) differences among all three age groups were observed for first appearance, last appearance, and for net period of visibility. For maxillary teeth there were significant differences among all three groups for first and for last appearance but only between the juvenile and the two adult groups for net period of visibility. Within all three groups, lesions on mandibular teeth appeared and disappeared significantly earlier than on maxillary teeth. Only in the oldest group were lesions visible for a significantly longer net period of time on mandibular teeth than on maxillary teeth.

DISCUSSION

The time sequences for the occurrence of the lesion and the incidence of rats with lesions in the 110-day group of the present study are similar to those for a previously reported group exposed to 230 rads at 101 days of age (Castanera, et al.). A minor differ-

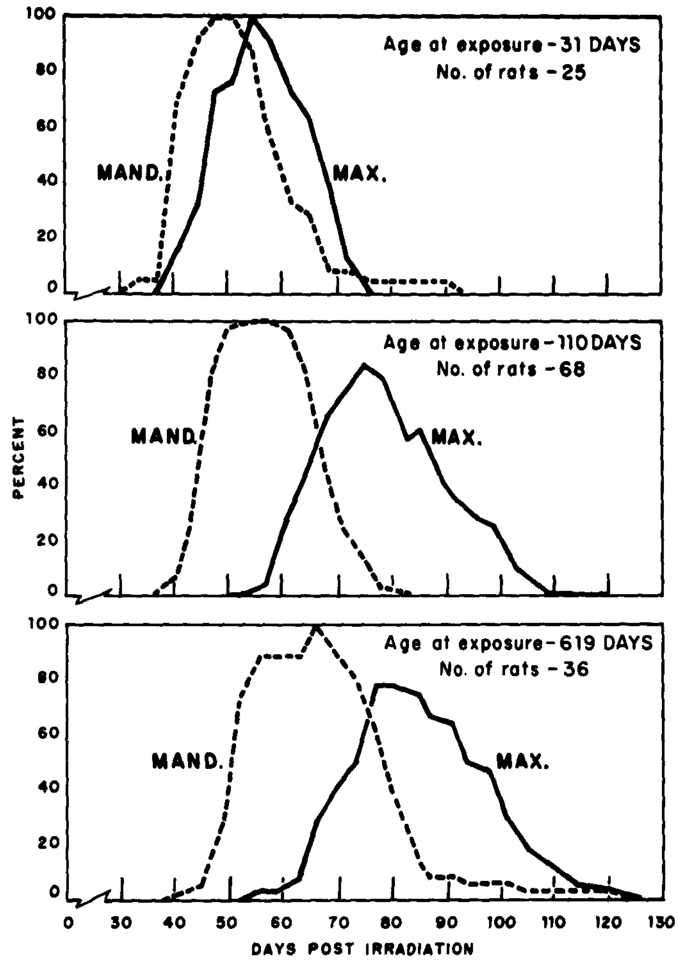

Fig. 2 Effect of age at exposure to 215 rads of fast neutrons upon period of visibility of incisor lesions. Rats with fractured incisors are excluded.

ence in fracture incidence between the two studies appears to be unremarkable, since fracture probably depends primarily upon the occurrence of incidental trauma.

From the results of the present study, it appears that the effects of age at irradiation upon the radiation-induced dental lesion are manifested in two ways. First, the severity of the structural defect is inversely related to age at irradiation. That is, younger animals exhibit a wider lesion and a greater incidence of broken incisors. This more intense response in younger animals could be related to more active tooth formation with relatively more tooth substance formed per unit time. The work of Medak et al. (1950) suggests that there is some decline in rate of tooth eruption with increasing age. If this were a major factor, one would expect to find a shorter net observation period for the visible lesion in younger animals as a result of a greater eruption rate since attrition tends to balance eruption so that tooth length remains relatively constant over short periods of time. Results of the present study are not inconsistent with this explanation, but the fact that younger animals have shorter incisors is also a significant point to consider (see below). Another factor in the greater severity of the dental lesion in younger animals may be inferred from the disruption of nutrition and metabolism caused by irradiation. It is interesting to speculate that the metabolic cost of the depression in food consumption commonly observed after doses in the high sublethal range may be much greater to the juvenile animal which is irradiated during a period of extremely rapid growth. Obviously, some combination of a direct effect upon the tooth forming tissues and a general systemic effect is quite likely.

The time sequence of the observable lesion is the second way in which the effects of age at irradiation are manifested. Radiation serves to mark that dental tissue formed during the radiation injury phase (Kimeldorf, et al., 1962). It appears that differences in time of first, last and net observation may be related principally to anatomic and/or eruption rate factors associated with age. For example, in juvenile animals, the earlier appearance and disappearance and the shorter period of observation may be related to a smaller distance from tooth bud to gingival crest and to a shorter length of visible incisor than in the adult animals. The differences in time patterns of the dental lesion in mandibular and maxillary incisors are probably due to a combination of anatomic and eruption rate factors since it is known that, at least in non-irradiated animals, maxillary incisors erupt at a slower rate than mandibular incisors (Ginn and Volker, 1944; Schour and Massler, 1949). In addition to anatomic and physiologic factors, genetic and/or neonatal effects appear to influence indices of odontogenesis since by the Kruskal-Wallis analysis of variance (Siegel, 1956) the mean day of first observation of the lesion varies significantly ($p < 0.001$) among litters within each age group.

SUMMARY

Male rats were irradiated with a high sublethal dose (215 rads) of fast neutrons at 31, 110, or 619 days of age. The typical radiation-induced dental lesion (a chalky zone extending the full width of the tooth) was observed in the exposed shafts of the incisors beginning in the second month post-irradiation. While all animals exhibited the lesion on all incisors, the character of the lesion and its time sequence varied markedly with age at irradiation. The severity of the radiation effect was greater in the youngest group, as indicated by a wider lesion and a greater incidence of animals with fractured incisors (68% vs 11 or 12% for the older groups). The time sequence of appearance, duration of visibility, and disappearance by attrition occurred earlier in younger animals. However, these temporal differences appear related primarily to anatomic and physiologic factors associated with age per se rather than to a differential intensity of radiation damage.

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